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타클로리무스와 사이클로스포린이 뇌세포에 미치는 영향

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Effect of Tacrolimus and Cyclosporine on the Cultured Brain Cell Viability

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Objectives : After the organ transplantation, some patients suffer from mild neurological symptoms such as tremor to severe complications including seizures and encephalopathy. Neurological side effects can be caused by tacrolimus and cyclosporine (CsA). However, the mechanisms of encephalopathy by cyclosporine A and tacrolimus are not fully understood. We studied the cytotoxicity of cyclosporin A and tacrolimus, focused on the viability and reactive oxygen species, using the glioma cell line.

Methods : Varying concentrations of CsA or tacrolimus were added to glioma cells, and incubated for 24 hours at 37℃. The cell viability was measured using 3- (4,5- dimethyl- thiazol- 2- yl)- 2,5- diphenyl- tetrazolin bromide (MTT). 2.5 mM CsA or tacrolimus was added to glioma cells, and incubated for 60 minutes at 37℃. The production of ROS evaluated by measuring the fluorescent product from the oxidation of an oxidant- sensitive 2′,7′- dichlorofluorescin using VICTOR3TM multilabel counter.

Results : Substantial morphological changes were observed in glioma cells when they were treated with CsA or tacrolimus. Cells were detached and floated to the top of the culture dish, and a monolayer was not formed. Under the CsA, the cell viability were as follows: 100±0.1% at the zero mM of CsA as a control, 64.3±18.5% ($p<0.05$ vs. control) at the 0.25mM, 61.3±12.0% ($p<0.01$ vs. control) at the 0.50 mM, 68.1±18.8% ($p<0.05$ vs. control) at the 2.5 mM, 62.4±24.5% ($p<0.05$ vs. control) at the 5.0 mM, and 68.6±19.5% ($p<0.05$ vs. control) at the 10.0 mM. Under the tacrolimus, the cell viability were as follows: 100±0.1% at the zero mM of tacrolimus as a control, 38.6±29.4% ($p<0.05$ vs. control) at the 0.25mM, 40.8±26.5% ($p<0.05$ vs. control) at the 0.50 mM, 43.7±21.7% ($p<0.05$ vs. control) at the 2.5 mM, 37.8±27.7% ($p<0.01$ vs. control) at the 5.0 mM, and 43.0±29.8% ($p<0.05$ vs. control) at the 10.0 mM. And there was no significant difference between CsA and tacrolimus in the cell viability under the same concentration. CsA or tacrolimus resulted in the production of the ROS in the glioma cells, and the production of the ROS was increased as the time of the exposure to CsA passes.

Conclusions : CsA or tacrolimus can cause the neurological side effect and encephalopathy after organ transplantation by their direct cytotoxic effect on brain cells.

Key Words : 타클로리무스, 사이클로스포린, 뇌세포
Tacrolimus, Cyclosporine, Brain cell